Lung Cancer:

Causes and Prevention

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CHAPTER 14

Lung Cancer in Japan: Effects of Nutrition and Passive Smoking

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ABSTRACT

Lung cancer is on a sharp increase in both men and women in Japan. Nonsmoking wives with smoking husbands were found to carry an elevated risk of lung cancer and ischemic heart disease by a large-scale cohort study, 1966-1981, for 265,118 adults in 29 Health Center Districts in Japan, the risk steadily going up with the increase in number of cigarettes smoked by the husband. In major cancers other than lung, no such risk elevation was observed. A nonsmoking husband with a smoking wife also showed an elevated risk of lung cancer. The risk-reducing effect of daily intake of green-yellow vegetables on lung cancer was observed for passive smoking just as for active smoking. Those women eating green-yellow vegetables daily showed a significantly lower risk of lung cancer from the passive influence of their husbands' smoking. Such risk reduction was not observed for ischemic heart disease. The observed results suggest that the influence of husband's smoking on nonsmoking wives in raising the risk of lung cancer is as a cancer promoter rather than a cancer initiator. This promoter hypothesis may explain why such continuous but low-dose exposure of passive smoking, which starts after adult age is reached, significantly elevates lung cancer risk in nonsmoking wives.

Key Words: **Japan, cohort study, passive smoking, lung cancer, ischemic heart disease, green-yellow vegetables, β-carotene, promoter, promoter-inhibitor**

Lung Cancer: Causes and Prevention.

Introduction

The mortality from lung cancer has been increasing rapidly in Japan (Figure 1). The number of deaths among males was 520 in 1947 and 17,555 in 1982, the corresponding number for females was 248 and 6661.

There exists little sign of a slowing down of the rate of increase, and the number of deaths from lung cancer are expected to exceed the number of deaths from stomach cancer in the near future. In parallel to this trend the number of cigarettes sold in Japan also has been on a sharp rise (Figure 1). The random sample survey conducted by the Tobacco Monopoly Corporation in 1982 revealed that currently 70.1% of adult males and 15.4% of adult females smoke in Japan.

The purpose of this chapter is to study the causative factors of lung cancer in Japan with special reference to the effect of passive smoking relative to the effect of active smoking. The possible influence of nutrition, β-carotene-rich green-yellow vegetables in particular, on the risk enhancing effect of active and passive smoking also is studied.

Methods

The materials of our ongoing large-scale cohort study for 265,118 adults aged 40 years and above in Japan were analyzed in detail to discover factors altering the

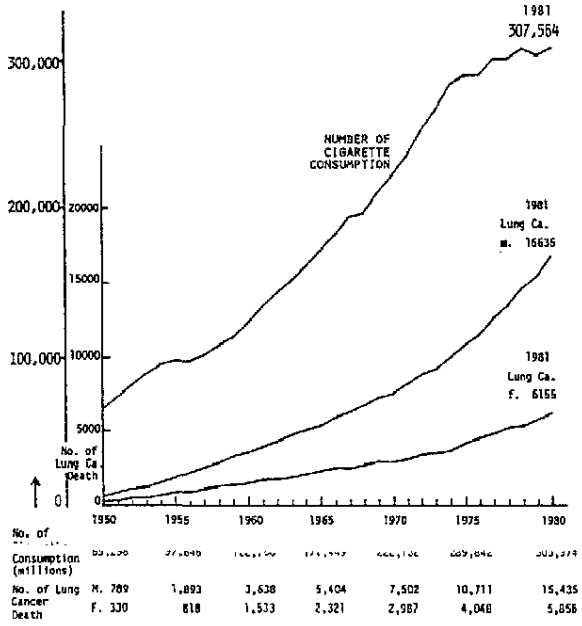

Figure 1. Trends in cigarette consumption and lung cancer deaths in Japan (1950–1981).

risk of lung cancer in both men and women. For statistical analysis, programs included in the book *Epidemiologic Analysis with a Programmable Calculator* (U.S. Department of Health, Education and Welfare, 1979) mainly were used.

Results

Active Smoking and Lung Cancer Risk

Cigarette smoking was identified by far the most important cause of lung cancer in Japan, both by case-control studies conducted by the author and other researchers and by a large-scale cohort study (1–6) being conducted by the author for 265,118 adults (122,261 men and 142,857 women) aged 40 and above (95% of census population) in 29 Health Center Districts in Japan. These subjects were surveyed in October–December 1965 and followed up from January 1966 until December 1981. A clear-cut dose-response relationship was observed between the number of cigarettes ever smoked and the age-standardized mortality rate of lung cancer. The mortality rate of lung cancer also was found to be higher the earlier smoking was begun when age and total number of cigarettes ever smoked were standardized (Figure 2). The lung cancer-standardized mortality rate was observed

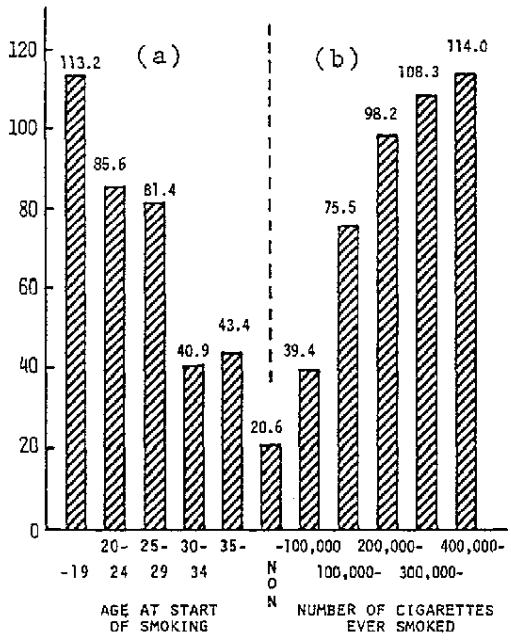

Figure 2. Lung Cancer. (a) Attained age- and amount of smoking-standardized mortality rate by age at start of smoking. (b) Attained age- and age at start of smoking-standardized mortality rate by total amount of cigarettes ever smoked. (Prospective study, 1966–1978 Japan.)

to be 18.3% lower in smokers who do not inhale compared to regular deep inhalers, and 48.9% lower in smokers of filtertip cigarettes compared to smokers of nonfiltertip cigarettes, according to our cohort study. The risk of lung cancer in daily smokers also was noted to approach gradually that of nonsmokers with the lapse of years after smoking cessation, risk difference diminishing by 41.6% in 5 years after stopping the habit. This strongly suggests the major part of the influence of smoking during adulthood is the promoter action of substances included in mainstream smoke.

Effect of Nutrition on Active Smokers

Daily intake of green-yellow vegetables, rich in β-carotene, was found significantly to lower the risk of lung cancer (7, 8), particularly when the total amount of cigarettes ever smoked was less than 300,000 (6) (Figure 3). No other dietary habit showed such risk reduction. Risk reduction after smoking cessation appeared to be more pronounced in case of daily consumers of green-yellow vegetables. Taking similar evidence in laboratory studies into consideration, a promoter-inhibitor interaction model was conceptualized.

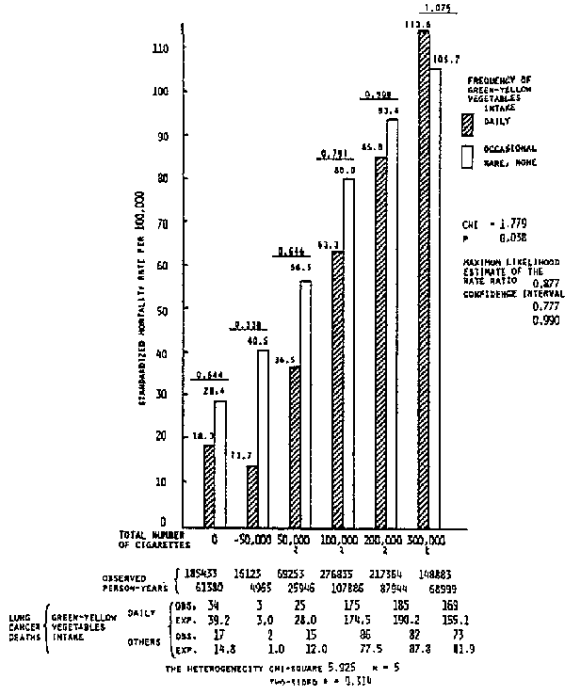

Figure 3. Standardized mortality rate for lung cancer by total number of cigarettes ever smoked and by frequency of green-yellow vegetable intake; males. (Prospective study, 1966-1978.)

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Figure 4. Age-
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Passive Smoking and Lung Cancer

In the present cohort study (1966–1981), 427 deaths from lung cancer in women were recorded during 16 years of followup (1966–1981). Of these women, 269 were married, and 200 of these also were nonsmokers. These cases occurred among 91,540 nonsmoking married women whose husbands' smoking habits were studied. The risk of lung cancer was carefully measured, taking into consideration possible confounding variables. There was a statistically significant increased risk in relation to the extent of the husband's smoking (Figure 4), which confirmed the validity of previous reports (9, 10). The association was significant when observed by age of husbands (Table 1, Figures 1 and 5) and also by age of wives (Table 2). The further detailed analysis on materials cross-tabulated by age and occupation of the husband also confirmed the association (Table 3). The husband's drinking habits were noted to have no effect in raising the risk of lung cancer in nonsmoking wives (Table 4).

Similar significant risk elevation of lung cancer with the increase in the extent of husband's smoking also was observed with ischemic heart disease when observed by husband's age and occupation (Tables 5 and 6). The significant risk elevation of cancer of the nasal sinus also was observed in nonsmoking wives with husband's smoking. The risk elevation of emphysema and chronic bronchitis with spouse's smoking also was noted with borderline significance. However there was no tendency of risk elevation at all in major cancers other than lung (total of cancers of stomach, cervix, and breast), the standardized mortality rate in nonsmoking wives being almost exactly the same regardless of the husband's smoking habit (Table 7, Figure 6).

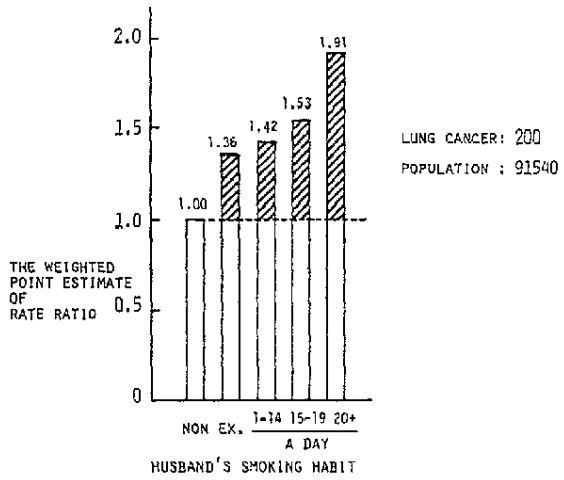

Figure 4. Age-standardized mortality rate ratio for lung cancer in nonsmoking wives by smoking habits of their husbands. (Prospective study, 1966–1981, Japan.)

Table 1. Mortality rate for lung cancer in women by age group and by smoking habit of husband (patient herself a nonsmoker): prospective study, 1966-1981, Japan[a]

Husband's age group	Husband's smoking habit: Nonsmoker No.	Nonsmoker Pop.	Ex-smoker No.	Ex-smoker Pop.	Number of cigarettes a day: 1-14/d No.	1-14/d Pop.	15-19/d No.	15-19/d Pop.	20+/d No.	20+/d Pop.	Total No.	Total Pop.
40-49	4	6,229	1	1,255	8	8,621	6	5,158	16	10,764	35	32,027
50-59	10	7,791	3	1,922	20	9,668	8	4,052	24	9,820	65	33,253
60-69	18	7,120	11	2,687	28	7,243	9	2,513	23	4,651	89	24,214
70-79	5	755	2	348	2	612	1	105	1	226	11	2,046
Total	37	21,895	17	6,212	58	26,144	24	11,828	64	25,461	200	91,540
[a]The weighted point estimate of rate ratio and test-based 90% confidence limits	1.00		1.36	2.18 0.85	1.42	2.01 1.01	1.58	2.38 0.98	1.91	2.71 1.34	Mantel extension χ^2 2.915 one-tail p value 0.00178	
						2.02 1.45						
								1.04				
Mantel-Haenszel χ^2	—		1.0855		1.8290				3.0295			
one-tail p value			0.1389		0.0337				0.0012			

Table 2. Mortality rate for lung cancer in nonsmoking wives by smoking habit of husbands and by age group of wife: prospective study; 1966-1981, Japan[a]

Wife's age group	Husband's smoking habit: Nonsmoker No.	Nonsmoker Pop.	Ex-smoker 1-19/d No.	Ex-smoker 1-19/d Pop.	Number of cigarettes a day: 20+/d No.	20+/d Pop.	Total No.	Total Pop.
40-49	4	7,918	21	17,492	21	12,615	46	38,025
50-59	14	7,635	46	15,640	31	8,814	91	32,089
60-69	16	6,170	31	10,381	10	3,793	57	20,344
70-79	3	172	1	671	2	239	6	1,082
Total	37	21,895	99	44,184	64	25,461	200	91,540
[a]The weighted point estimate of rate				2.01		2.55		
based 90% confidence limits				0.99		1.19	Mantel extension χ^2 2.424	
Mantel-Haenszel χ^2	—		1.6042		2.3731		one-tail p value 0.00768	
one-tail p value			0.0543		0.0088			

Table 3. Mc
of husbands (

Husbands age (year)
40-49
50-59
60-69
70 +

[a]Standardized Risk Ratios

[b]Occupation: 1, sales workers; 5 in transport and workers; 10, no

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Table 3. Mortality rate for lung cancer in women by age, occupation, and smoking habit of husbands (patient herself a nonsmoker)[a]

Husbands age (year)	Occupation[b]	Nonsmoker		Ex-smoker or 1–19/day		≥20/day	
		No.	Pop.	No.	Pop.	No.	Pop.
40–49	Total	4	6,229	15	15,034	16	10,764
	1		324		653	1	566
	2		90		231		293
	3	1	908	2	2,247	3	1,867
	4	1	476	1	993		1,044
	5	1	2,502	6	5,941	9	3,636
	6		46		165		108
	7		177	1	486	1	426
	8		1,112	3	3,431	2	2,241
	9		162	1	345		243
	10	1	432	1	542		340
50–59	Total	10	7,791	31	15,642	24	9,820
	1	1	345		593	2	446
	2		175		253	1	319
	3	1	817	5	1,764	1	1,324
	4	1	653	2	1,133	5	1,092
	5	4	3,497	16	6,812	9	3,514
	6		35		89		50
	7		120		273	1	234
	8	3	1,375	6	3,478	2	2,155
	9		164		378	1	251
	10		610	2	869	2	435
60–69	Total	18	7,120	48	12,443	23	4,651
	1		227	1	327	1	179
	2	1	91		143		124
	3		305	2	594	2	327
	4	2	508	5	822	1	500
	5	13	4,084	33	6,845	10	2,152
	6		9		31		14
	7		45		82		55
	8	1	805	5	1,784	4	736
	9		121	1	208		92
	10	1	925	1	1,607	5	472
70 +	Total	5	755	5	1,065	1	226
	1		32		30		5
	2		21		14		4
	3		18	1	36		8
	4		48		73		20
	5	3	323	1	446		89
	6		1		1		0
	7		1		5		1
	8		87	2	119	1	36
	9		11		19		2
	10	2	213	1	322		61
[a]Standardized Risk Ratios		1.000		1.436		1.872	

Mantel extension χ^2: 3.124; one-tail p value: 0.00089.

[b]Occupation: 1, Professional and technical workers; 2, managers and officials; 3, clerical and related workers; 4, sales workers; 5, farmers, lumbermen, and fishermen; 6, workers in mining and quarrying occupations; 7, workers in transport and communication occupations; 8, craftsmen, production process workers, and laborers; 9, service workers; 10, not classifiable and not reported.

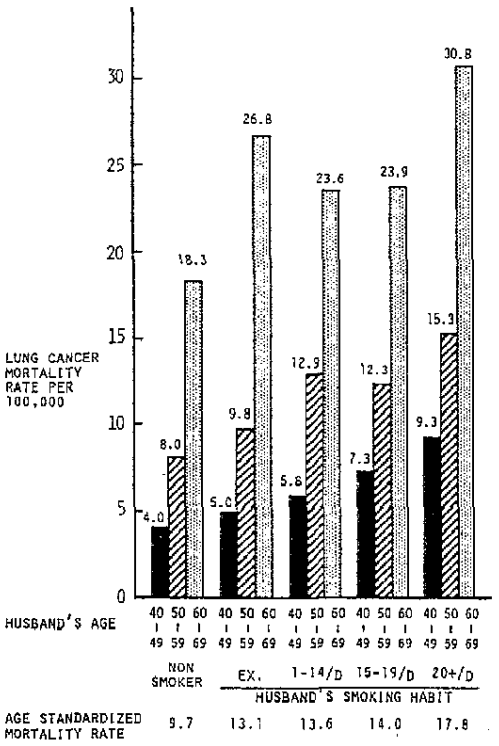

Figure 5. Age-specific mortality rate for lung cancer per 100,000 in nonsmoking wives by smoking habits of their husbands. (Prospective study, 1966–1981, Japan.)

Table 4. Mortality rate for lung cancer in women by age group and by alcohol drinking habits of husband: (patient herself a nonsmoker); prospective study, 1966–1981, Japan

Husband's age group	Husband's drinking habits: Nondrinker No.	Nondrinker Pop.	Occas. Rare No.	Occas. Rare Pop.	Daily No.	Daily Pop.	Obscure No.	Obscure Pop.	Total No.	Total Pop.
40–49	12	6,141	10	15,877	13	9,935	0	74	35	32,027
50–59	12	7,437	29	14,666	24	10,786	0	364	65	33,253
60–69	23	6,741	35	9,234	27	7,606	4	633	89	24,214
70–79	1	686	5	666	4	589	1	105	11	2,046
Total	48	21,005	79	40,443	68	28,916	5	1,176	200	91,540
The weighted point estimate of rate				1.61		1.59				
ratio and test-based 90% confidence limits		1.00		1.03 0.66		1.11 0.77				
Mantel-Haenszel χ^2 one-tail p value	—			=0.1019 0.4594		0.4564 0.3240			Mantel extension χ^2 0.626 one-tail p value 0.26566	

Table 5. Mortality rate for ischemic heart diseases in women by age group and by smoking habits of husband: prospective study, 1966–1981, Japan

	Husband's smoking habit							
			Number of cigarettes a day					
	Nonsmoker		Ex-smoker 1-19/d		20+/d		Total	
Husband's age group	No.	Pop.	No.	Pop.	No.	Pop.	No.	Pop.
40–49	13	6,229	40	15,034	33	10,764	86	32,027
50–59	26	7,791	56	15,642	49	9,820	131	33,253
60–69	65	7,120	125	12,443	47	4,651	237	24,214
70–79	14	755	19	1,065	7	226	40	2,046
Total	118	21,895	240	44,184	136	25,461	494	91,540
The weighted point estimate of rate ratio and test-based 90% confidence limits	1.00		1.10	1.33 0.91	1.31	1.63 1.06		
Mantel-Haenszel χ^2 one-tail p value	—		0.8504 0.1976		2.0723 0.0191		Mantel extension χ^2 2.073 one-tail p value 0.01909	

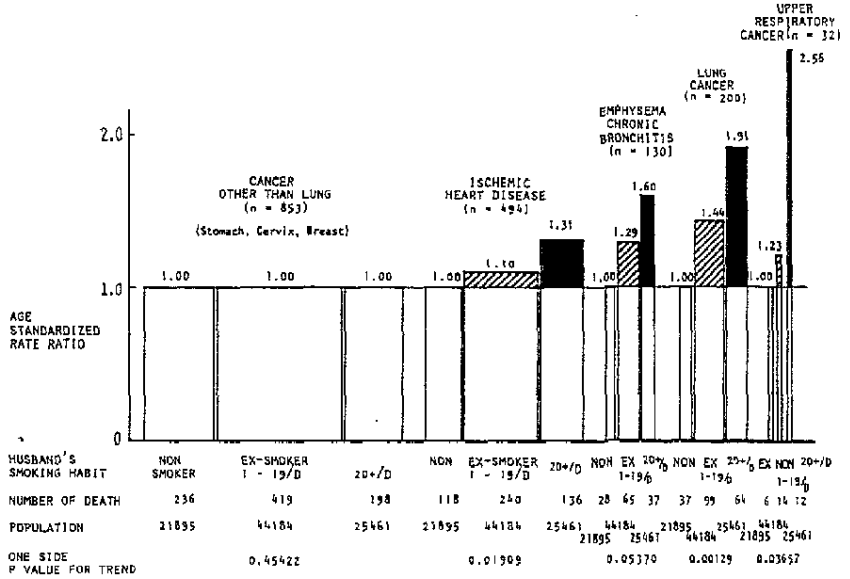

Figure 6. Standardized mortality rate ratio for selected causes of death in 91,540 nonsmoking women by smoking habits of their husbands. (Prospective study, 1966–1981, Japan.)

Table 6. Mortality rate for ischemic heart disease in women by age, occupation, and smoking habit of husbands (patient herself a nonsmoker)[a]

Husbands age (years)	Occupation[b]	Nonsmoker		Ex-smoker or 1–19/day		≥20/day	
		No.	Pop.	No.	Pop.	No.	Pop.
40–49	Total	13	6,229	40	15,034	33	10,764
	1	1	324		653	1	566
	2		90	1	231		293
	3		908	4	2,247	1	1,867
	4		476	1	993	5	1,044
	5	8	2,502	25	5,941	18	3,636
	6		46		165		108
	7	1	177	2	486		426
	8		1,112	7	3,431	6	2,241
	9		162		345	1	243
	10	3	432		542	1	340
50–59	Total	26	7,791	56	15,642	49	9,820
	1	1	345	3	593		446
	2	2	175		253		319
	3	2	817	5	1,764	6	1,324
	4		653	6	1,133	4	1,092
	5	15	3,497	27	6,812	26	3,514
	6		35	1	89		50
	7		120	1	273	2	234
	8	5	1,375	8	3,478	11	2,155
	9		164	1	378		251
	10	1	610	4	869		435
60–69	Total	65	7,120	125	12,443	47	4,651
	1	2	277	2	327	1	179
	2	1	91	2	143	1	124
	3	2	305	5	594	1	327
	4	10	508	8	822	5	500
	5	36	4,084	79	6,845	27	2,152
	6		9	1	31		14
	7	1	45	1	82	1	55
	8	7	805	13	1,784	6	736
	9	1	121	2	208		92
	10	5	925	12	1,607	5	472
70+	Total	14	755	19	1,065	7	226
	1	2	32	1	30		5
	2	2	21		14	1	4
	3		18	1	36		8
	4	1	48	1	73		20
	5	5	323	11	446	2	89
	6		1		1		0
	7		1		5		1
	8		87	1	119	3	36
	9		11	2	19		2
	10	4	213	2	322	1	61
[a] Standardized Risk Ratios		1.000		1.103		1.359	

Mantel extension χ^2: 2.351; one-tail p value: 0.00936.

[b] Occupation: 1, Professional and technical workers; 2, managers and officials; 3, clerical and related workers; 4, sales workers; 5, farmers, lumbermen, and fishermen; 6, workers in mining and quarrying occupations; 7, workers in transport and communication occupations; 8, craftsmen, production process workers, and laborers; 9, service workers; 10, not classifiable and not reported.

Table 7a. by smokin 1981, Jap

Husband's age group
40–49
50–59
60–69
70–79
Total

[a] The weighte estimate of r ratio and tes based 90% confidence li

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Husbands age (years)
40–49
50–59
60–69

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Table 7a. Mortality rates for major cancers other than lung in women by age group and by smoking habit of husband (patient herself a nonsmoker): prospective study, 1966–1981, Japan[a]

Husband's age group	Husband's smoking habit (cigarettes a day)							
	Nonsmoker		Ex-smoker 1–19		20+		Total	
	No.	Pop.	No.	Pop.	No.	Pop.	No.	Pop.
40–49	44	6,229	117	15,034	71	10,764	232	32,027
50–59	97	7,791	191	15,642	119	9,820	407	33,253
60–69	160	7,120	274	12,443	106	4,651	540	24,214
70–79	14	755	20	1,065	8	226	42	2,046
Total	315	21,895	602	44,184	304	25,461	1,221	91,540
[a]The weighted point estimate of rate ratio and test-based 90% confidence limits	1.00		1.00 (1.11, 0.90)		1.00 (1.05, 0.95)			
Mantel-Haenszel χ^2 one-tail p value	—		−0.0015 0.4994		0.0449 0.4821		Mantel extension χ^2 0.115 one-tail p value 0.4542	

Table 7 b. Mortality rates for major cancers other than lung in women by age, occupation, and smoking habit of the husband (patient herself a nonsmoker)[a]

Husbands age (years)	Occupation[b]	Nonsmoker		Ex-smoker or 1–19/day		≥20/day	
		No.	Pop.	No.	Pop.	No.	Pop.
40–49	Total	45	6,229	120	15,034	74	10,764
	1	2	324	1	653	3	566
	2		90	1	231	2	293
	3	9	908	17	2,247	12	1,867
	4	3	476	8	993	8	1,044
	5	17	2,502	59	5,941	35	3,636
	6		46		165		108
	7	1	177	6	486		426
	8	10	1,112	21	3,431	13	2,241
	9	1	162	4	345	1	243
	10	2	432	3	542		340
50–59	Total	98	7,791	195	15,642	122	9,820
	1	13	345	2	593	3	446
	2	2	175	1	253	1	319
	3	14	817	16	1,764	10	1,324
	4	1	653	18	1,133	9	1,092
	5	49	3,497	81	6,812	56	3,514
	6		35		89		50
	7	2	120	4	273	2	234
	8	12	1,375	49	3,478	31	2,155
	9		164	7	378	4	251
	10	5	510	17	669	6	435
60–69	Total	161	7,120	227	12,443	106	4,651
	1	5	227	5	327	2	179
	2	5	91	3	143	3	124
	3	7	205	11	559	5	327
	4	5	508	28	822	12	500
	5	102	4,084	158	6,845	58	2,152

Table 7 b. (cont.)

Husbands age (years)	Occupation[b]	Nonsmoker No.	Nonsmoker Pop.	Ex-smoker or 1–19/day No.	Ex-smoker or 1–19/day Pop.	≥20/day No.	≥20/day Pop.
	6		9	1	31		14
	7	1	45	3	82	2	55
	8	10	805	40	1,784	17	736
	9	2	121	3	208		92
	10	24	925	25	1,607	7	472
70 +	Total	14	755	21	1,065	8	226
	1		32		30		5
	2	1	21		14		4
	3	1	18		36		8
	4		48	1	73	2	20
	5	7	323	15	446	4	89
	6		1		1		0
	7		1		5		1
	8	1	87	2	119	1	36
	9		11		19		2
	10	4	213	3	322	1	61
[a]Standardized Risk Ratios		1.000		0.969		1.034	

Mantel extension χ^2: −0.129; one-tail p value: 0.44868.

[b]Occupation: 1, Professional and technical workers; 2, managers and officials; 3, clerical and related workers; 4, sales workers; 5, farmers, lumbermen, and fishermen; 6, workers in mining and quarrying occupations; 7, workers in transport and communication occupations; 8, craftsmen, production process workers, and laborers; 9, service workers; 10, not classifiable and not reported.

Comparison of the Effects of Active Smoking and Passive Smoking

When the risk of lung cancer in nonsmokers with nonsmoking spouses was taken as a unit, a definite dose–response relationship was observed, the highest risk being in heavy active smokers, followed by mild active smokers, then heavy passive smokers, and then mild passive smokers (Figure 7). The risk gradient was similar both in men and in women (Figure 8). A significantly elevated risk of lung cancer also was noted for nonsmoking husbands with smoking wives.

Because the size of population exposed to passive smoking is quite large in the case of women, the effect of passive smoking because of the husband's smoking was estimated as 65% of that of active smoking. Our recent survey showed that 47.5% and 32.6% of Japanese adult women were being exposed to passive smoking at home and at the workplace, respectively (Figure 9). Therefore it must be a sound estimate that the total effect of passive smoking is approximately equivalent to that of active smoking in women. However, as a majority of adult men are still smokers, the total effect of passive smoking relative to active smoking must be on

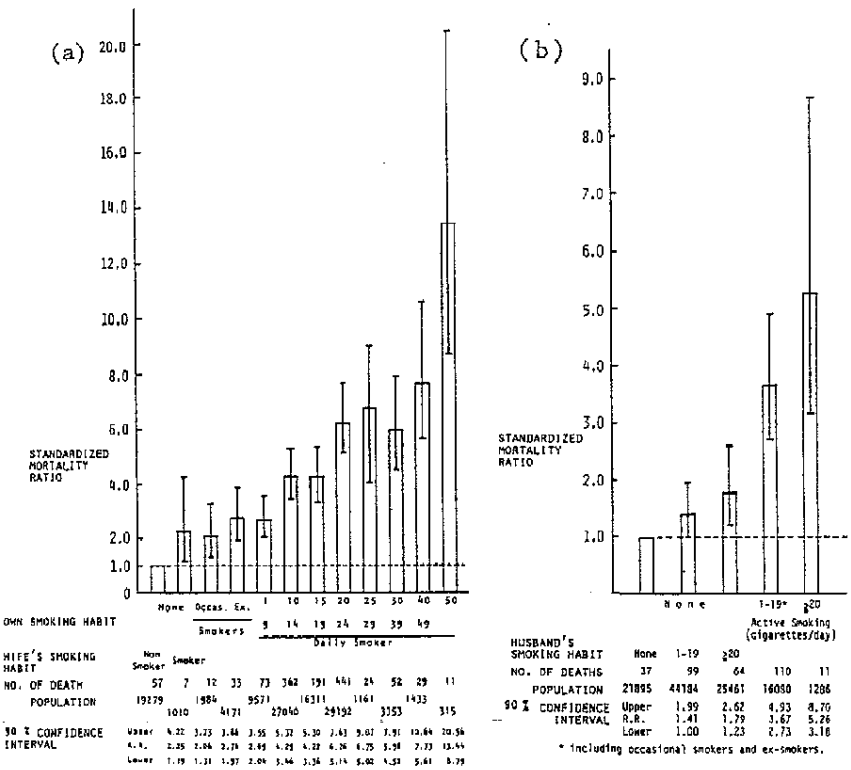

Figure 7. (a) Active and passive smoking and lung cancer mortality: relative risks (RR) with 90% confidence intervals; males.(Prospective study, 1966–1981, Japan.) (b) Active and passive smoking and lung cancer mortality: relative risks (RR) with 90% confidence intervals; females. (Prospective study, 1966–1981, Japan.)

the order of a few percent. The effect on lung cancer risk of passive smoking at home in relation to active smoking for men was calculated as 0.4% in our series.

Effect of Nutrition on Passive Smokers

A significantly lower risk of lung cancer was observed when nonsmoking wives with smoking husbands consumed green-yellow vegetables daily (Tables 8 and 9, Figures 10 and 11) suggesting that the promoter-inhibitor interaction model also applied to passive smoking just as in active smoking (Figure 9). Such risk reduction caused by daily intake of green-yellow vegetables was not observed for ischemic heart disease (Table 10, Figure 12).

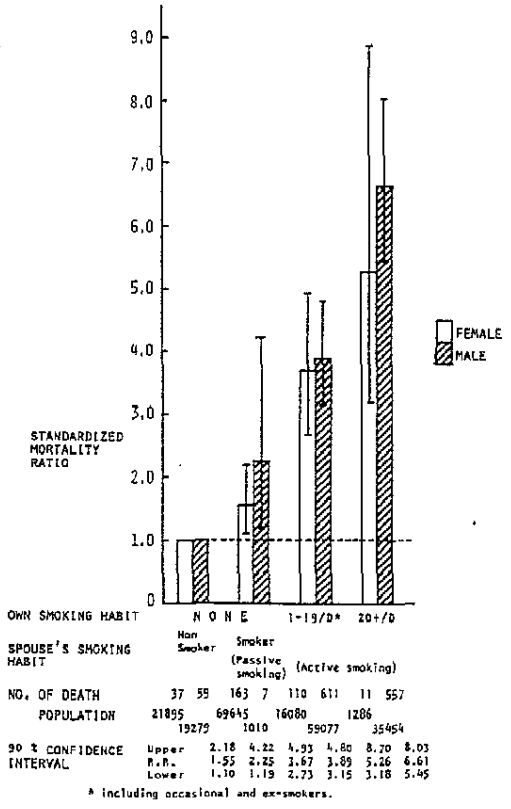

Figure 8. Active and passive smoking and lung cancer mortality: relative risks (RR) with 90% confidence intervals. (Prospective study, 1966–1981, Japan.)

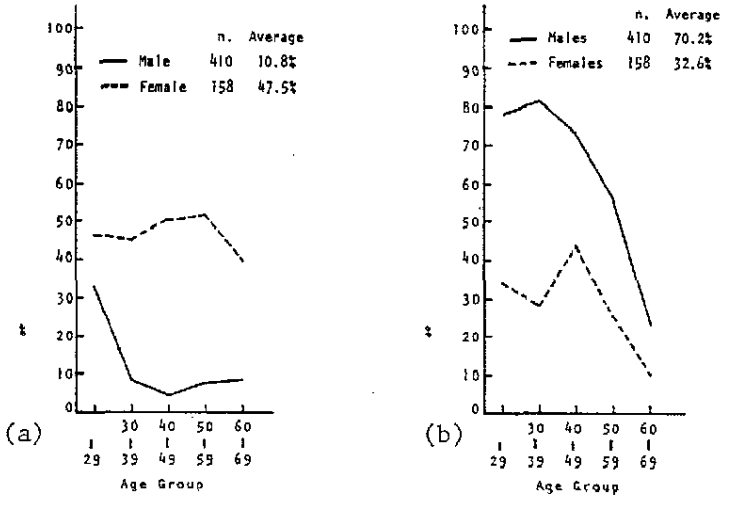

Figure 9. (a) Percentage of nonsmokers exposed to sidestream smoke at home, Japan, 1983. (b) Percentage of nonsmokers exposed to sidestream smoke at the workplace, Japan, 1983.

Table 8. Lung cancer mortality rate in nonsmoking wives by smoking habit of the husband: comparison be-

Table 8. Lung cancer mortality rate in nonsmoking wives by smoking habit of the husband: comparison between daily and non daily intake of green-yellow vegetables

Husband's smoking habits		Nonsmoker				Ex-smoker on 1-19 day				≥20/day			
Wife's eating habits		Green-yellow vegetables											
		Daily		Nondaily		Daily		Nondaily		Daily		Nondaily	
Husband's		Pop.	Lung Ca.	Pop.	Lung Ca.	Pop.	Lung Ca.	Pop.	Lung Ca.	Pop.	Lung Ca.	Pop.	Lung Ca.
Occupation	Age												
Agriculture	40–49	1,958	1	544	0	5,050	5	891	1	3,037	7	599	2
	50–59	2,805	4	692	0	5,196	11	1,616	5	2,588	9	926	0
	60–69	3,359	7	725	6	5,106	22	1,739	11	1,588	6	564	4
	70–79	258	3	65	0	287	1	159	0	45	0	44	0
Others	40–49	2,422	3	1,305	0	7,288	8	1,805	1	5,377	5	1,751	2
	50–59	3,181	5	1,113	1	6,732	12	2,098	3	4,633	5	1,673	10
	60–69	2,266	4	770	1	4,088	9	1,510	6	1,906	10	593	3
	70–79	216	2	216	0	371	1	248	3	81	1	56	0
Total		16,465	29	5,430	8	34,118	69	10,066	30	19,255	43	6,206	21

Grand total	Population: 91540	Lung cancer: 200

Green-yellow vegetables	Mantel-extension χ^2	P-value (two tailed)
Daily	2.072	0.03827
Nondaily	2.487	0.01288
Total	3.090	0.00200

Table 9. Effect of daily intake of green-yellow vegetables on lung cancer mortality in nonsmoking wives with smoking husbands[a]

Husband's smoking habit		Ex-smoker or 1–19/day				≥20/day			
Wife's eating habit		Green-yellow vegetables							
		Daily		Nondaily		Daily		Nondaily	
Husband's		Pop.	Lung Ca.	Pop.	Lung Ca.	Pop.	Lung Ca.	Pop.	Lung Ca.
Occupation	Age								
Agriculture	40–49	5,050	5	891	1	3,037	7	559	2
	50–59	5,196	11	1,616	5	2,588	9	926	0
	60–69	5,106	22	1,739	11	1,588	6	564	4
	70–79	287	1	159	0	45	0	44	0
Others	40–49	7,288	8	1,805	1	5,377	5	1,751	2
	50–59	6,732	12	2,098	3	4,633	5	1,673	10
	60–69	4,088	9	1,510	6	1,906	10	593	3
	70–79	371	1	248	3	81	1	56	0
Total		34,118	69	10,056	30	19,255	43	6,206	21

[a]Mantel-Haenszel χ^2: −1,986; p (two-tailed 0.047). Odds ratio: Nondaily green-yellow vegetable intaker, 1,000; daily green-yellow vegetables intake, 0.707 (standardized rate ratio); 90% confidence limits, 0.538–0.943.

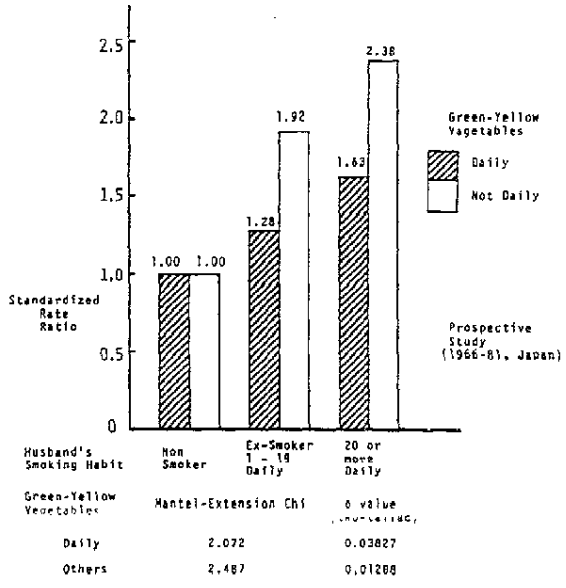

Figure 10. Lung cancer mortality ratio in nonsmoking wives by smoking habits of their husbands. Comparison between daily and nondaily intake of green-yellow vegetables.

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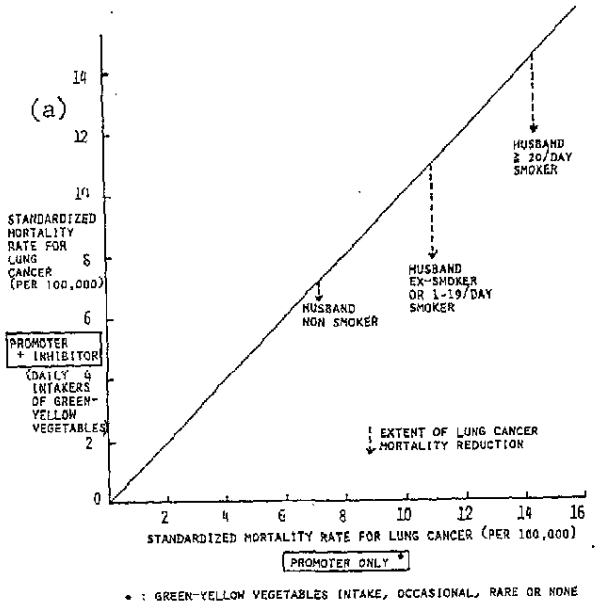

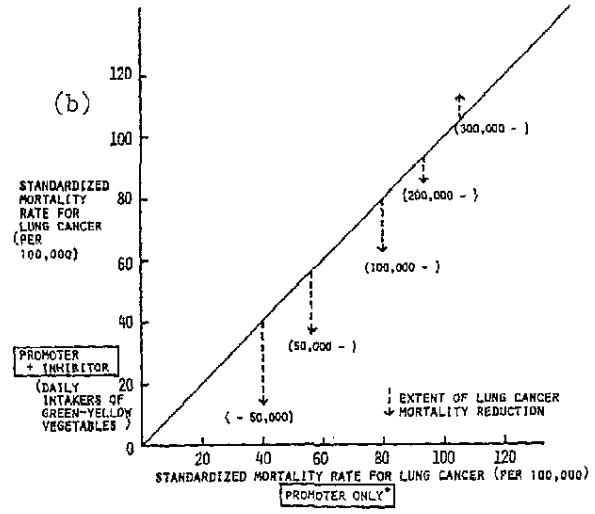

Figure 11. (a) Standardized mortality rate for lung cancer in nonsmoking wives by smoking habit of the husband. Comparison between daily and nondaily intake of green-yellow vegetables. (Prospective study, 1966–1981, Japan.) (b) Standardized mortality rate for lung cancer according to total number of cigarettes smoked and frequency of consumption of green-yellow vegetables; males. (Prospective study, 1966–1978, Japan.)

Table 10. Ischemic heart disease mortality rate in nonsmoking wives by smoking habit of the husband: comparison between green-yellow vegetables intake daily and nondaily

Husband's smoking habit		Nonsmoker				Ex-smoker or 1–19/day				≥ 20/day			
Wife's eating habit		Green-yellow vegetables											
		Daily		Nondaily		Daily		Nondaily		Daily		Nondaily	
Husband's		Pop.	Ischemic Heart D.	Pop.	Ischemic Heart D.	Pop.	Ischemic Heart D.	Pop.	Ischemic Heart D.	Pop.	Ischemic Heart D.	Pop.	Ischemic Heart D.
Occupation	Age												
Agriculture	40–49	1,958	6	544	2	5,050	18	891	7	3,037	14	599	4
	50–59	2,805	11	692	4	5,196	25	1,616	2	2,588	21	926	5
	60–69	3,359	30	725	6	5,106	55	1,739	24	1,588	21	564	6
	70–79	258	2	65	3	287	10	159	1	45	2	44	0
Others	40–49	2,422	3	1,305	2	7,288	10	1,805	5	5,377	12	1,751	3
	50–59	3,181	8	1,113	3	6,732	18	2,098	11	4,633	17	1,673	6
	60–69	2,266	21	770	8	4,088	33	1,510	13	1,906	11	593	9
	70–79	216	7	216	2	371	6	248	2	81	3	56	2
Total		16,465	88	5,430	30	34,118	175	10,066	65	19,255	101	6,206	35
Grand total		Population: 91540				Ischemic heart disease: 494							
Green yellow vegetables		Mantel-extension χ^2				P value (two tailed)							
Daily		2.307				0.02105							
Nondaily		0.820				0.41222							
Total		2.406				0.01613							

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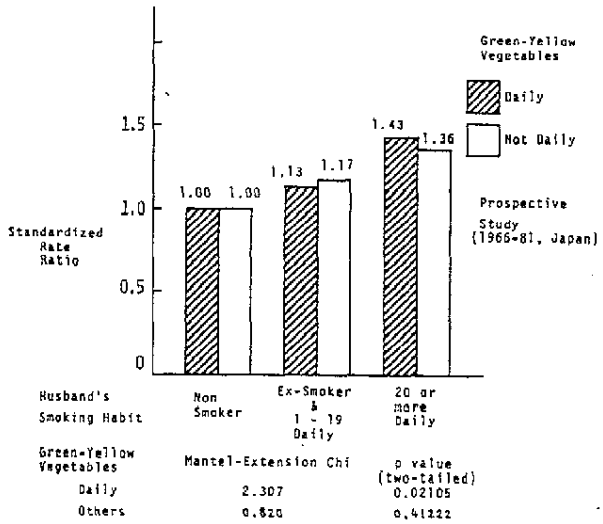

Figure 12. Ischemic heart disease mortality ratio in nonsmoking wives by smoking habits of their husbands. Comparison between daily and nondaily intake of green-yellow vegetables.

Discussion

The age-adjusted mortality rates for lung cancer have been sharply increasing both for men and for women in Japan. As only a fraction of Japanese women with lung cancer smoke cigarettes, the reasons for the trend of their mortality from lung cancer have been unclear. The present study appears to explain at least a part of this long-standing riddle.

This observation also questions the validity of the conventional method of assessing the relative risk of developing lung cancer in smokers by comparing them with nonsmokers. This study shows that nonsmokers are not a homogeneous group and should be subdivided according to the extent of previous exposure to indirect or passive smoking. Although the relative risk of indirect smoking was smaller than that of direct smoking, the absolute excess deaths from lung cancer resulting from passive smoking must be important because of the large size of the exposed group. Therefore, these results of our current study must be of public health importance, strengthening already existing evidence for a health hazard from passive smoking (11-15) (Table 11).

As shown in Figure 9, 47.5% and 32.6% of 158 nonsmoking adult women surveyed recently are noted to be exposed to sidestream smoke at home and at the workplace, respectively. One survey conducted in Aichi prefecture in Japan showed that nonsmoking wives are exposed to their husband's smoking 6.7 times a day on the average.

Because sidestream smoke contains varieties of cancer promoters at higher concentration than does mainstream smoke, it must be reasonable to consider the

Table 11. Passive smoking is harzardous to health

1. Existence of toxic substances (including carcinogens) in sidestream smoke mostly at higher concentration than in mainstream smoke.
2. Existence of a large number of nonsmokers who have to inhale sidestream smoke frequently and intensively for long years at home and/or at the workplace.
3. Existence of sidestream smoke component in blood and urine of nonsmokers exposed to passive smoking, (eg, nicotine, CO-Hb in blood and Mutagens in urine.).
4. Existence of functional abnormalities in nonsmokers exposed heavily to passive smoking (eg, respiratory or circulatory function).
5. Lung tissue damage and destruction in chronic passive smokers as shown by elevated hydroxyproline excretion in urine.
6. Higher incidence of selected diseases in nonsmokers exposed heavily to passive smoking (eg, pneumonia, bronchitis, asthma, ischemic heart disease, lung and nasal sinus cancer).
7. Experimental evidence.

main effect of passive smoking on lung cancer risk results from the prolonged exposure to such promoters in sidestream smoke. The risk-inhibitory effect of a daily intake of green-yellow vegetables that are rich in β-carotene must be considered as an additional evidence for such a promoter action hypothesis of passive smoking. The hypothesis also explains why exposure to passive smoking that starts after reaching adult age can significantly influence the risk of lung cancer.

The histology of 21 cases of lung cancer in nonsmoking wives of smoking husbands was not essentially different from that in smoking women (adenocarcinoma 57.1%, squamous cell carcinoma 19.0%, and small-cell carcinoma 4.8%). A case-control study conducted within our cohort study revealed a significant dose-response relationship between adenocarcinoma of the lung and the number of cigarettes smoked daily, relative risk being 1.39 and 5.75 for smokers of 1–14 and 15 or more cigarettes daily, the chi square for the trend being 6.848 with a one-tail p value of 0.004. Therefore the predominance of adenocarcinoma of the lung in nonsmoking women with smoking husbands should not be considered unfavorable evidence for promoter action hypothesis of passive smoking. In passive smoking, sidestream smoke usually is inhaled through the nose, whereas in active smoking mainstream smoke always is inhaled through the mouth. This difference could be a reason for the elevated risk of nasal sinus cancer in passive smokers. The mechanism of the action of passive smoking on the risk of ischemic heart disease, however, must be explained in different ways (eg, a combined action of carbon monoxide and nicotine).

In summary, to reduce the effect of active and passive smoking and to encourage the effect of nutrition, in particular β-carotene intake, would be the most productive course for lung cancer prevention. For selected persons exposed to other known carcinogens, eg, those related to occupation or radiation, such environmental exposure also must be minimized in addition to the preventive measures focused on lifestyle variables given above.

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